

Journal of Advances in Medicine and Medical Research

31(11): 1-4, 2019; Article no.JAMMR.53639 ISSN: 2456-8899 (Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

The Imaging Features of Isocitrate Dehydrogenase Mutant Gliomas

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

Article Information

DOI: 10.9734/JAMMR/2019/v31i1130334 <u>Editor(s):</u> (1) Dr. Muhammad Torequl Islam, Assistant Professor, Department of Pharmacy, Faculty of Life Science, Bangabandhu Sheikh Mujibur Rahman Science and Technology University, Bangladesh and Researcher, Ton Duc Thang University, Vietnam. <u>Reviewers:</u>

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 Complete Peer review History: http://www.sdiarticle4.com/review-history/53639

Review Article

Received 05 November 2019 Accepted 10 January 2020 Published 23 January 2020

ABSTRACT

To appraise Magnetic resonance imaging features of isocitrate dehydrogenase (IDH) mutant gliomas. In literature, IDH mutant gliomas are usually in frontal lobes, they are less contrastenhancing with well-defined borders. They have high ADC values low regional cerebral blood volumes. 2-HG detection of MR spectroscopy has more promising results. In this review, we tried to describe conventional and advanced neuroimaging features of IDH mutant Gliomas.

Keywords: Glioma; IDH; mutant; MRI; MR spectroscopy; MR perfusion.

1. INTRODUCTION AND LITERATURE EVIDENCE

The revised World Health Organization (WHO) 2016 classification [1] subdivides grades II, III and IV Diffuse gliomas into isocitrate dehydrogenase (IDH) mutant and IDH wild-type glioma. WHO grade II and III gliomas, as well as in secondary glioblastoma usually show

mutations [2]. Recent studies revealed that IDH mutant gliomas show favourable positive effects on survival and chemosensitivity [3,4]. The Gold standard for detecting mutations are the immunohistochemistry and genomic sequence analysis. The disadvantage is, these methods are invasive and sometimes biopsy leads to erroneous results due to tumour heterogeneity. The lesion heterogeneity sometimes reduces the

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yield of biopsy and genomic analysis. This heterogeneity provides opportunities for medical imaging procedures that can assess the entire lesion in a noninvasive and reproducible way. This is the reason, a non-invasive and accurate method such as MRI with variable imaging protocols is highly valuable to predict IDH mutation. Different MRI sequences have great potential in routine clinical practice and these could be of great help with the implementation of appropriate procedures in patients with diffuse gliomas [5].

Magnetic resonance imaging (MRI) has proved a vital non-invasive modality of choice for examining gliomas. Recently, multiple studies reported on the imaging features and the great analytic performance of MRI for extrapolation of IDH mutation in patients with glioma [6-16].

The various MRI modalities have been used. including conventional MRI as well as advanced techniques such as diffusion-weighted imaging (DWI) or perfusion-weighted imaging (PWI). Also. detection of oncometabolite 2hydroxyglutarate on MRS has been introduced images of sensitive for detection of IDH mutation [17]. Currently, the radionics approaches using quantitative imaging features have been successfully used in detecting IDH mutation [18]. Therefore, the purpose of our review is to restate the imaging features of IDH mutant glioma and highlight the analytic performance of MRI for

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prediction of IDH mutation in patients with diffuse gliomas.

2. LITERATURE EVIDENCE

There are several studies which used conventionally as well as advanced features to predict IDH mutation.

As shown in Table 1, the features of frontal lobe location [14,19,20,21,22,23], less contrast [14,20,24,25,26] with well defined borders [27,28] are more predictive of mutation. Other features such as T2 FLAIR mismatch [29] and Other features such as T2 FLAIR mismatch and high ADC values are also in favour of IDH mutation [30,31].

To simplify it, these authors state that IDH mutant lesions are usually in the frontal lobes as compared to the non-mutant ones. The mutant lesions are less vascular with well-defined borders.

Also, Advanced imaging such as DTI, perfusion and spectroscopy provide a clue in a reliable fashion. The IDH mutant glioma does not show a destructive pattern on diffusion tensor imaging (DTI) and fractional anisotropy(FA) value is significantly lower in mutant glioma than wildtype gliomas [30,31,28]. On PWI, several studies consistently proved that IDH mutant glioma showed lower relative cerebral blood volume (rCBV) values and lower tumour blood flow (rCBF) than IDH wild-type gliomas [31,28].

Table 1. Conventional MR features

MR features/Main Findings	Studies by
Frontal lobe location	Nakae S, Murayama K, Sasaki H, et al., Lasocki A, Tsui A,
	Gaillard, et al, Delfanti RL, Piccioni DE, Handwerker J, et,
	Wasserman JK, Nicholas G, Yaworski R, et al., Sonoda Y,
	Shibahara I, Kawaguchi T, et al., Reyes-Botero G, Dehais C,
	Idbaih A, et al, Carrillo JA, Lai A, Nghiemphu PL, et al.
Less contrast enhancement	Nakae S, Murayama K, Sasaki H, et al., Lasocki A, Tsui A,
	Gaillard, et al, Wang K, Wang Y, Fan X, et al, Choi C, Raisanen
	JM, Ganji SK, et al., de la Fuente MI, Young RJ, Rubel J, et al.
Well defined borders	Delfanti RL, Piccioni DE, Handwerker J, et al.
T2 FLAIR mismatch	Patel SH, Poisson LM, Brat DJ, et al.
High ADC values	Xing Z, Yang X, Leu K, Ott GA, Lai A, et al., 31, Wasserman JK,
-	Nicholas G, Yaworski R, et al, Price SJ, Allinson K, Liu H, et al.

Table 2. Advanced MR features

MR features	Studies by
DTI minimally invasive	Tan W, Xiong, et al.
FA map low values	Lee S, Choi ŠH, Ryoo I, et al
Low relative cerebral blood flow	Xing Z, Yang X, 34, Leu K, Ott GA, Lai A, et al, de la Fuente
	MI, Young RJ, Rubel J, et al
2 hydroxyglutarate MRS	Xiong J, Tan W, Wen J, et al

The quantitative evaluation using 2hydroxyglutarate MRS [19] requires dedicated software and is also a reliable method for IDH mutation.

3. CONCLUSION

IDH mutant gliomas show less aggressive behaviour as compared to wild-type gliomas. MR has significant potential to non-invasively give the clue about mutation and 2hydroxyglutartae MRS has significantly highsensitivity than other sequences.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

- Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: A summary. Acta Neuropathol. 2016;131:803–820.
- 2. Hartmann C, Meyer J, Balss J, et al. Type and frequency of IDH1 and IDH2 mutations are related to astrocytic and oligodendroglial differentiation and age: A study of 1,010 diffuse gliomas. Acta Neuropathol. 2009;118:469–474.
- Brat DJ, Verhaak RG, Aldape KD, et al. Comprehensive, Integrative Genomic Analysis of Diffuse Lower-Grade Gliomas. N Engl J Med. 2015;372:2481–2498.
- Eckel-Passow JE, Lachance DH, Molinaro AM, et al. Glioma groups based on 1p/19q, IDH, and TERT promoter mutations in tumours. N Engl J Med. 2015;372:2499– 2508.
- Zhou H, Vallieres M, Bai HX, et al. MRI features predict survival and molecular markers in diffuse lower-grade gliomas. Neuro Oncol. 2017;19:862–870
- Zhang B, Chang K, Ramkissoon S, et al. Multimodal MRI features predict isocitrate dehydrogenase genotype in high-grade

gliomas. Neuro Oncol. 2017;19:109–117.

- Yu J, Shi Z, Lian Y, et al. Noninvasive IDH1 mutation estimation based on a quantitative radiomics approach for grade II glioma. Eur Radiol 2017;27:3509– 3522.
- Xing Z, Yang X, She D, Lin Y, Zhang Y, Cao D. Noninvasive assessment of IDH mutational status in World Health Organization grade II and III astrocytomas using DWI and DSC-PWI combined with conventional MR imaging. AJNR Am J Neuroradiol. 2017;38:1134–1144.
- Tietze A, Choi C, Mickey B, et al. Noninvasive assessment of isocitrate dehydrogenase mutation status in cerebral gliomas by magnetic resonance spectroscopy in a clinical setting. J Neurosurg. 2018;128:391–398.
- Tan W, Xiong J, Huang W, Wu J, Zhan S, Geng D, Noninvasively detecting Isocitrate dehydrogenase 1 gene status in astrocytoma by dynamic susceptibility contrast MRI. J Magn Reson Imaging. 2017;45:492–499.
- Stadlbauer A, Zimmermann M, Kitzwogerer M, et al. MR Imaging-derived oxygen metabolism and neovascularization characterization for grading and IDH gene mutation detection of gliomas. Radiology. 2017;283:799–809.
- 12. Price SJ, Allinson K, Liu H, et al. Less invasive phenotype found in isocitrate dehydrogenase-mutated glioblastomas than in isocitrate dehydrogenase wildtype glioblastomas: A diffusion tensor imaging study. Radiology. 2017;283:215– 221.
- Patel SH, Poisson LM, Brat DJ, et al. T2-FLAIR mismatch, an imaging biomarker for IDH and 1p/19q status in lower-grade gliomas: A TCGA/TCIA project. Clin Cancer Res. 2017;23:6078–6085.
- Nakae S, Murayama K, Sasaki H, et al. Prediction of genetic subgroups in adult supratentorial gliomas by pre- and intraoperative parameters. J Neurooncol. 2017;131:403–412.
- Lasocki A, Tsui A, Gaillard F, Tacey M, Drummond K, Stuckey S. Reliability of noncontrast-enhancing tumour as a biomarker of IDH1 mutation status in glioblastoma. J Clin Neurosci. 2017; 39:170–175.
- 16. Jiang S, Zou T, Eberhart CG, et al. Predicting IDH mutation status in grade II

gliomas using amide proton transferweighted (APTw) MRI. Magn Reson Med. 2017;78:1100–1109.

- 17. Choi C, Ganji SK, DeBerardinis RJ, et al. 2-hydroxyglutarate detection by magnetic resonance spectroscopy in IDH-mutated patients with gliomas. Nat Med 2012;18: 624–629.
- Li Z, Wang Y, Yu J, Guo Y, Cao W. Deep Learning-based Radiomics (DLR) and its usage in noninvasive IDH1 prediction for low-grade glioma. Sci Rep. 2017;7:5467.
- Xiong J, Tan W, Wen J, et al. Combination of diffusion tensor imaging and conventional MRI correlates with isocitrate dehydrogenase 1/2 mutations but not 1p/19q genotyping in oligodendroglial tumours. Eur Radiol. 2016;26:1705–1715.
- Lasocki A, Tsui A, Gaillard F, Tacey M, Drummond K, Stuckey S. Reliability of noncontrast-enhancing tumor as a biomarker of IDH1 mutation status in glioblastoma. J Clin Neurosci. 2017; 39:170–175.
- Sonoda Y, Shibahara I, Kawaguchi T, et al. Association between molecular alterations and tumor location and MRI characteristics in anaplastic gliomas. Brain Tumor Pathol. 2015;32:99–104.
- 22. Reves-Botero G, Dehais C, Idbaih A, et al. Contrast enhancement in 1p/19qcodeleted anaplastic oligodendrogliomas is genomic associated with 9p loss, instability, and angiogenic gene expression. Neuro Oncol. 2014;16:662-670.
- Carrillo JA, Lai A, Nghiemphu PL, et al. Relationship between tumor enhancement, edema, IDH1 mutational status, MGMT promoter methylation, and survival in glioblastoma. AJNR Am J Neuroradiol. 2012;33:1349–1355.
- 24. Delfanti RL, Piccioni DE, Handwerker J et al. Imaging correlates for the 2016 update

on WHO classification of grade II/III gliomas: implications for IDH, 1p/19q and ATRX status. J Neurooncol. 2017;135: 601–609.

- 25. Wang K, Wang Y, Fan X, et al. Radiological features combined with IDH1 status for predicting the survival outcome of glioblastoma patients. Neuro Oncol. 2016;18:589–597.
- Choi C, Raisanen JM, Ganji SK, et al. Prospective longitudinal analysis of 2hydroxyglutarate magnetic resonance spectroscopy identifies broad clinical utility for the management of patients with IDHmutant glioma. J Clin Oncol. 2016;34: 4030–4039.
- 27. Wasserman JK, Nicholas G, Yaworski R, et al. Radiological and pathological features associated with IDH1-R132H mutation status and early mortality in newly diagnosed anaplastic astrocytic tumours. PLoS One. 2015;10:e0123890.
- Yamashita K, Hiwatashi A, Togao O et al (2MR imagingbased analysis of glioblastoma multiforme: Estimation of IDH1 mutation status. AJNR Am J Neuroradiol. 2016;37:58–65.
- 29. Leu K, Ott GA, Lai A, et al. Perfusion and diffusion MRI signatures in histologic and genetic subtypes of WHO grade II–III diffuse gliomas. J Neurooncol. 2017; 134:177–188
- Lee S, Choi SH, Ryoo I, et al. Evaluation of the microenvironmental heterogeneity in high-grade gliomas with IDH1/2 gene mutation using histogram analysis of diffusion-weighted imaging and dynamicsusceptibility contrast perfusion imaging. J Neurooncol. 2015;121:141–150.
- Tan W, Xiong J, Huang W, Wu J, Zhan S, Geng D, Noninvasively detecting Isocitrate dehydrogenase 1 gene status in astrocytoma by dynamic susceptibility contrast MRI. J Magn Reson Imaging. 2017;45:492–499.

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